



## POSITION PAPER ON THE AVAILABILITY OF EQUINE MEDICINES

### Members

Austria  
Belgium  
Denmark  
Finland  
France  
Germany  
Greece  
Iceland  
Ireland  
Italy  
Luxembourg  
Netherlands  
Norway  
Portugal  
Spain  
Sweden  
Switzerland  
United Kingdom

### Observers

Croatia  
Czech Republic  
Estonia  
FYROM  
Hungary  
Latvia  
Lithuania  
Poland  
Slovak Republic  
Slovenia  
Yugoslavia

### Sections

Practitioners  
State Officers  
Industry and Research  
Hygienists

### SUMMARY

Equine veterinary practitioners are confronted with the reduction in the number of the products lawfully available to treat horses, which has impaired the quality of treatment of life-threatening conditions such as colic.

This situation results from the ever increasing resources required for the development of pharmaceutical products; resources that pharmaceutical companies are no longer willing to invest when the market share is too small, as it is indeed the case for the equine market.

In addition, despite the fact that only a limited number of horses are each year slaughtered in the Community to enter the food-chain, the horse is considered as a food-producing animal. This implies that specific additional studies must be carried out to assess the potential impact on the consumer of the residues of any product used in horses. Extra investments are therefore required which again are too high compared to the market share.

This paper gives an overview of the situation today as far as the availability of medicines for horses is concerned and makes proposals to restore the therapeutic arsenal required by equine practitioners whilst also ensuring the protection of public health.

#### President

Dr K. Simon

#### Vice-Presidents

Dr H. Lundström  
Dr C. Mir  
Dr F. Orozco

## INTRODUCTION: FACTS AND FIGURES

Veterinarians have the obligation to protect public health from potential harmful residues of veterinary medicinal products. They also need to have medicinal products to protect animal health and animal welfare. Many of the requirements for the placing on the market of veterinary medicinal products, which are intended to protect public health, have however resulted in the limitation of a number of products available to equine practitioners to protect animal health and animal welfare.

One might then wonder whether these measures do not go beyond what is necessary to achieve their purpose, whether these measures are properly designed to manage the risk associated with the use of veterinary medicinal products and to protect public health from harmful residues.

As far as horses are concerned the following preliminary points should therefore be considered: What are the quantity of equine meat eaten each year in the Community? What proportion of the equine population might enter the food-chain?

It is difficult to find information on the number of horses kept in the European Community as well as on the number of those slaughtered each year to enter the food-chain.

Data presented in Annex I however indicates that the three major area of production and consumption of equine meat in the European Union are represented by the Benelux, France and Italy.

Most of the ca. 370 000 horses slaughtered each year in the European Union are indeed slaughtered in these countries as indicated by the following figures.

- There are between 60 000 and 100 000 horses in Belgium<sup>1</sup>. In 1992, 9 000 horses were slaughtered<sup>2</sup>. In 1997, 2 373 tons of fresh meat were produced in Belgium, for an average consumption of horse meat of 1.8 kg per person per year<sup>3</sup>.
- There are between 200 and 300 000 horses live in the Netherlands. 2 700 horses were slaughtered in 1996.
- 350 000 horses were recorded in France in 1995. 37 000 horses were slaughtered, representing 9 200 tons of fresh meat. One third of the horses slaughtered in France are imported. Mainly from Poland. 30 700 tons of equine fresh meat were imported, 60% of which from the US and Argentina.<sup>4</sup> 6 000 tons were exported. The average consumption of horse meat was 0.6 kg per person<sup>5</sup> in 1995, compared to 38 kg of porcine meat and 30 kg of bovine meat.
- In Italy, 240 000 horses were slaughtered in 1993, representing 60 000 tons of fresh meat. 16 400 tons of fresh meat were also imported.

---

<sup>1</sup>Personnal communication from the Ministère des Classes Moyennes et de l'Agriculture.

<sup>2</sup>Annuaire statistique de la Belgique (1994). Institut National des Statistiques. Ministère des Affaires Economiques.

<sup>3</sup>Office Interprofessionnel des Viandes de l'Elevage et de l'Aviculture

<sup>4</sup>Productions des IAA en 1993. Enquête des branches agricoles. Ministère de l'Agriculture de de la Forêt.

<sup>5</sup>L'agriculture, la forêt et les industries agro-alimentaires. Ministère de l'Agriculture, de la Pêche et de l'Alimentation (1997).

In other Member States, like Germany (650 000 horses), the UK (565 000), Sweden (170 000) or Denmark (100 000) horses are almost exclusively kept for recreational activities.

Finally, the total consumption of equine meat of the EU is 168 000 tons which represent less than 0.5 kg per person.

#### **Meat consumption in the EU**

	Equine	Chicken	Porcine	Bovine	Ovine
Total Consumption (1000 x tons)	168	7809	15236	7141	1373
Total consumption per capita (kg)	0.4	20.8	40.6	19	3.7

Office Interprofessionel des Viandes de l'Élevage et de l'Aviculture

These figures clearly indicate that the vast majority of equines in the Community are kept for recreational purposes and that, even in those countries where equine meat is consumed, it represents only a fraction of the total meat consumption. Horses are however considered as food-producing animals as a result of Community law.

#### **HORSES ARE CONSIDERED AS FOOD-PRODUCING ANIMALS**

EU legislation<sup>6</sup> provides that the Official Veterinarian must declare unfit for human consumption any meat containing residues of veterinary medicinal products if such residues exceed the permitted level laid down by Community rules. This applies to meat from domestic solipeds (e.g. horses) in exactly the same way as other meat from, more conventional, food-producing animals.

As a consequence, no distinction is made upstream in the production chain between recreational horses and those bred for meat production only. A number of recreational horses are indeed slaughtered and enter the food chain at the end of their life.

All horses being considered food-producing animals, the use of veterinary medicinal products becomes conditional upon additional requirements intended to protect public health: maximum residue limits must be established for those molecules used in horses (see Annex II).

---

<sup>6</sup>Council Directive 64/433/EEC on health problems affecting intra-Community trade in fresh meat.

## THE SITUATION TODAY

Many measures have been taken to harmonise the requirements for the granting of a marketing authorisation and to establish procedures to give new products a quick access to the market (see Annex III). However, despite these efforts, the number of substances for which MRLs have been established today for horses is very limited and the number of products which have been granted a marketing authorisation for use in horses is even more limited (see Annex IV and V). Indeed the cost of producing a data package for the establishment of an MRL and for bringing new products onto the market is such that it limits the number of products available to practitioners. For horses, as for many other minor species or minor uses, the market is too small to provide pharmaceutical companies with a fair return on their investment, hence the hesitations of companies to develop new products.

For the same reasons, pharmaceutical companies are also not always willing to invest resources to have MRLs established for those old substances which were already authorised in 1992 and which are under review by the CVMP. Some of the older products might therefore disappear from the market between now and January 2000.

The withdrawal of old products and the paucity of new replacement products give a gloomy prospect for the therapeutic arsenal available to the practitioner at the beginning of the new millennium.

Of course Directive 81/851 provides that where no authorised product for a condition exists, the Member States may exceptionally, in particular to avoid causing unacceptable suffering to the animal concerned, permit the administration of another product by a veterinarian to an animal or a small number of animals. This is known as the cascade system.

However, because this exception is subject to many conditions, and because the horse is considered as a food-producing animal, the equine practitioner can in practice not use products other than those authorised for horses.

Some life-threatening conditions, such as shock and colic can hardly be treated today, as the most essential products to treat such conditions (e.g. analgesics, gaseous anaesthetics, intravenous fluids, cardiac stimulants or medicines affecting the gastrointestinal region) are not always available. This situation might be worse tomorrow if some of the old products used by practitioners disappear from the market as a result of the MRL Regulation.

In such cases, when no product is available in their country to treat a particular condition, equine practitioners have no alternative but to use non authorised products, if the animal is to be treated at all. It might then be a product authorised for use in horses in another Member State but not in their own; or a product authorised in their country but not for horses (the so-called off-label use). In the absence of relevant data but having nevertheless to prescribe, practitioners must then in both cases assume complete responsibility for their therapeutic choice.

## **SITUATION IN EU MAJOR TRADE PARTNERS**

In the United States of America, the number of horses slaughtered decreased from 250 000 in the early nineties to 100 000 in 1996<sup>7</sup>. Their carcasses are almost exclusively for export to the EU.

In the US, horses are not considered as food-producing animals. Thus, pharmaceutical companies are not required to establish MRLs for substances used in horses.

In addition, when no equine medicine exists which contains the needed ingredient or is presented in the proper dosage form or is labelled for the indication or is clinically effective, practitioners may use extralabelly any other drug available, animal or human. (see Annex V).

Spot samples from horses sent to the slaughter house are randomly taken to monitor residues. When residues are present above permitted levels, the owner of the animal is held responsible except when the veterinarian failed to provide information about the waiting period to be observed.

The situation in Canada and South America, two other major horse meat exporting countries to the EU, is comparable to that in the US.

A great number of horse meat is however imported in the form of live animals which are then slaughtered in the EU. One of the conditions for the import of horses from third countries is that those horses are clearly and indelibly marked by a hot-branded 'S' of not less than 3 cm size on the hoof of the left front leg<sup>8</sup>.

## **MEASURES ALREADY TAKEN TO MAINTAIN AVAILABILITY OF EQUINE MEDICINES**

A few Member States have already taken steps to maintain the quality of treatment in allowing the use of products, for which no MRLs have been established in horses not intended for human consumption.

Such an approach will undoubtedly facilitate the registration by pharmaceutical companies of new products intended for horses not intended for human consumption. It will also allow practitioners to make full use of the so-called cascade system.

However, the use of such products in horses, provided that these horses are not intended for human consumption, causes problem as there is today no mechanism to control this. In addition, this is creating a double standard between imported horses, which could have been treated with any drug during their life, and horses raised in the EU.

---

<sup>7</sup>Personal communication from the American Association of Equine Practitioners.

<sup>8</sup>Commission Decision 93/196/EEC of 5 February 1993 on animal health conditions and veterinary certification for imports of equidae for slaughter.

## **PROPOSALS**

### **Horses are primarily kept for sport or leisure purposes**

Firstly, it must be recognised that in the EU horses are primarily kept for sport or leisure purposes. It must also be recognised that horses may become food-producing animals, either at birth or subsequently.

When a horse becomes a food-producing animal and is to be slaughtered for human consumption then a set of rules must be followed in order to protect consumers from possible harmful residues.

### **Reliable foolproof identification**

Firstly all horses and critically food-producing horses must be individually identified.

This could be done by visual identification or by a mark, either external (e.g. ear tag) or internal (e.g. microchip, tattoo...).

### **Pre-slaughter waiting period**

To guarantee that horses, treated with products not intended for food-producing animals, do not cause public health concerns when entering the human food-chain, a pre-slaughter waiting period must be respected. This period should be long enough to ensure depletion of residues below levels of any concern to public health. However, during this period, horses could still be treated with products for which MRLs have been established.

### **Certification**

Compliance with this pre-slaughter waiting period, should be monitored by means of a certificate issued by the veterinary surgeon taking care of the animal.

Thus, if owners of horses, previously treated with products not authorised for food-producing animals, are willing to send their animals to the slaughterhouse, these horses must first be identified as food-producing animals and a certificate issued at the same time by the veterinarian.

This certificate would include the identification of the animal, the date when the animal was registered as food-producing animal and the date from when the animal can be slaughtered and enter the food chain.

### **Control at the slaughterhouse**

At the slaughterhouse, no horse would be allowed to enter the food chain for human consumption unless it is identified, it is accompanied by the certificate issued by the veterinarian and the pre-slaughter waiting period has been respected.

## CONCLUSIONS

If no distinction is made by Member States and the EU legislator between horses raised for the purpose of meat production and recreational horses, the veterinary profession will be denied access to many drugs for alleviating the suffering of recreational horses. Whilst harming veterinary medicine and creating an animal welfare problem, these measures seem disproportionate, as in many cases, these horses will never end up on the consumer's plate, or will do so after such a time that any residues would have by then disappeared.

Therefore, considering the limited number of recreational horses which are slaughtered and enter the food chain every year in the Europe Union, the Federation of Veterinarians in Europe considers that a distinction must be made between recreational horses and food-producing horses.

Such a distinction is unlikely to have any negative impact on public health, if all food-producing horses are identified and accompanied by documents at the slaughterhouse. These two measures would together indeed offer a reliable and traceable means to ensure that the pre-slaughter waiting period is observed for those former recreational horses entering the food-chain for human consumption.

These proposals, in trying to conciliate animal health, animal welfare and public health, take full account of risk assessment and risk management principles. The Federation of Veterinarians of Europe therefore believes that they might be a way forward to restore and maintain the therapeutic arsenal of equine practitioners while ensuring that consumers are still adequately protected from harmful residues of veterinary medicinal products.

Finally, other more general measures could be developed such as a list of essential products and incentives to increase the number of products intended for minor species and minor uses. These measures are discussed in the FVE discussion paper on medicines availability for minor species and minor uses (FVE/98/026).

## ANNEX I

### Production of equine fresh meat in the EU

1000 x tons	1990	1992	1997*
Belgium	1	1	2.3
Denmark	1	2	1
Germany	4	1.6	4.2
Greece	0.2	0	0.1
Spain	6.9	7.3	8
France	10.2	10.1	9.9
Ireland	0	0	0
Italy	15	22	13.5
Netherlands	3	2	2.1
Portugal	1	1	0.7
UK	0	2	0.8
<b>Total (12)</b>	<b>42.3</b>	<b>47</b>	<b>42.6</b>
<b>Total (15)</b>			<b>45.5</b>

\* Estimate

Office Interprofessionel des Viandes de l'Elevage et de l'Aviculture

### Consumption of equine fresh meat in the EU

1000 x tons	1990	1992	1997*
Belgium	30	21	18.1
Denmark	1	1	1
Germany	4.5	4.9	6.8
Greece	0	0	0
Spain	7	7.9	8.3
France	57.7	48.2	36.8
Ireland	0	0	0
Italy	76	78	72.3
Netherlands	21	21	18.1
Portugal	1	1	0.5
UK	0	0	0
<b>Total (12)</b>	<b>198.2</b>	<b>183</b>	<b>161.9</b>
<b>Total (15)</b>			<b>168.5</b>

\* Estimate

Office Interprofessionel des Viandes de l'Elevage et de l'Aviculture

## ANNEX II

### **MAXIMUM RESIDUE LIMITS MUST BE ESTABLISHED FOR ALL SUBSTANCES CONTAINED IN VETERINARY MEDICINAL PRODUCTS INTENDED FOR USE IN FOOD-PRODUCING ANIMALS**

In order to protect public health, the Community has adopted measures to establish the level of residues, which can be accepted in foodstuffs without constituting a hazard to the health of the consumer. In particular, Council Regulation (EEC) No 2377/90 lays down a procedure for the establishment of maximum residue limits (MRLs) of veterinary medicinal products in foodstuffs of animal origin.

This Regulation stipulates that MRLs must be established for any substance intended for use in food-producing animals prior to its use in the Community. For substances, which were already used in food-producing animals before the entry into force of this Regulation (1 January 1992), there is an ongoing transitional process, at the end of which (1 January 2000) MRLs would also have been established. If not, products intended for food-producing animals and containing these substances would have to be withdrawn from the market.

For the establishment of MRLs, pharmaceutical companies must submit applications supported by specific data relating to the pharmacological and toxicological profile of the substance, as well as the results of residue depletion studies in the species for which the substance is intended.

Such applications must be submitted to the European Agency for the Evaluation of Medicinal Products (EMEA), where they are evaluated by the Committee for Veterinary Medicinal Products (CVMP). Eventually, the recommendation of the CVMP is transmitted to the European Commission, which turns it into Community law.

Substances are then classified in one of the four annexes of Regulation 2377/90:

- Annex I lists substances for which maximum residue limits have been established.
- Annex II contains those substances for which it is not necessary for the protection of public health to establish a maximum residue limit.
- Annex III lists substances for which provisional maximum residue limits have been established, whilst the sponsor company is carrying out further studies. Inclusion in this Annex is however conditional on the absence of any grounds for supposing that residues at the level proposed may present a hazard to the health of the consumer.
- The residues of some substances constitute a hazard to the consumer at whatever limit. Such substances are therefore prohibited in the Community for use in veterinary medicinal products intended for food-producing species and are listed in Annex IV.

### ANNEX III

#### AUTHORISATION FOR THE PLACING ON THE MARKET OF VETERINARY MEDICINAL PRODUCTS

Besides the establishment of MRLs, Community legislation requires that no veterinary medicinal product may be placed on the market of a Member State unless a marketing authorisation has been issued<sup>9</sup>. To obtain such authorisations, pharmaceutical companies must submit an application to:

- the EMEA, via the so-called centralised Community procedure, whereby the company could obtain a Community marketing authorisation valid throughout the Community. This procedure is, however, currently limited to products derived from biotechnology, to innovative products or to products containing a new active substance;
- Member States' competent authorities, via the so-called decentralised Community procedure, whereby the company could obtain national marketing authorisations. This procedure relies on the mutual recognition by Member States of the first marketing authorisation granted by one of them;
- a single Member State, if the product is to be marketed in this Member State only. Otherwise if the product is to be marketed in more than one Member State, the company must use one of the two Community procedures outlined above.

This application must contain the results of tests and trials demonstrating that the product has met with the required standards of quality, safety and efficacy<sup>10</sup>, including maximum residue limits for food-producing animals.

---

<sup>9</sup>Council Directive 81/851/EEC of 28 September 1981 on the approximation of the laws of Member States relating to veterinary medicinal products.

<sup>10</sup>Council Directive 81/852/EEC of 28 September 1981 on the approximation of the laws of Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of veterinary medicinal products.

## ANNEX IV

### Maximum Residue Limits for New Substances adopted by the Community since 1.1.1995

(Status: January 1999)

Substance a) INN	Therapeutic area a) Target species	EMEA/CVMP a) Validation b) Opinion c) Active time d) Clockstop	Commission a) Sent to Commission b) Date of the regulation c) OJ No.
a) Difloxacin	a) Chicken, turkeys	a) 16.05.95 b) 15.12.95 c) 134 days d) 49 days	a) 13.02.96 b) 08.07.96 c) OJ No. L 170 of 09.07.96
a) Ketoprofen (extension)	a) Porcine	a) 15.05.95 b) 22.03.96 c) 85 days d) 217 days	a) 25.04.96 b) 06.09.96 c) OJ No. L 226 of 07.09.96
a) Diclazuril	a) Ovine	a) 12.12.95 b) 24.04.96 c) 104 days d) 0	a) 24.05.96 b) 21.10.96 c) OJ No. L 269 of 22.10.96
a) Eprinomectin	a) Bovine	a) 22.02.96 b) 25.06.96 c) 108 days d) 0	a) 26.07.96 b) 08.01.97 c) OJ No. L 5 of 09.01.97
a) Doramectin (modification)	a) Bovine	a) 14.05.96 b) 24.07.96 c) 70 days d) 0	a) 23.08.96 b) 14.02.97 c) OJ No. L 45 of 15.02.97
a) Praziquantel	a) Ovine	a) 03.08.95 b) 18.09.96 c) 187 days d) 152 days	a) 16.10.96 b) 25.04.97 c) OJ No. L 110 of 26.04.97
a) Moxidectin (modification)	a) Bovine and Ovine	a) 12.06.96 b) 18.09.96 c) 97 days d) 0	a) 16.10.96 b) 25.04.97 c) OJ No. L 110 of 26.04.97
a) Difloxacin (modification)	a) Chicken, Turkeys	a) 10.07.96 b) 23.10.96 c) 104 days d) 0	a) 19.11.96 b) 25.04.97 c) OJ No. L 110 of 26.04.97
a) Ivermectin (extension)	a) Deer	a) 20.08.96 b) 11.12.96 c) 86 days d) 0	a) 09.01.97 b) 23.04.97 c) OJ No. L 106 of 24.04.97
a) Amitraz (extension)	a) Bees	a) 18.10.96 b) 12.02.97 c) 115 days d) 0	a) 12.03.97 b) 24.09.97 c) OJ No. L 263 of 25.09.97
a) Doramectin (extension)	a) Swine and Ovine	a) 10.06.96 b) 12.02.97 c) 118 days d) 127 days	a) 12.03.97 b) 24.09.97 c) OJ No. L 263 of 25.09.97
a) Cefzolin (extension)	a) Ovine and Caprine	a) 05.06.97 b) 10.09.97 c) 97 days d) 0	a) 10.10.97 b) 16.01.98 c) OJ No. L 11 of 17.01.98

<b>Substance</b> a) INN	<b>Therapeutic area</b> a) Target species	<b>EMEA/CVMP</b> a) Validation b) Opinion c) Active time d) Clockstop	<b>Commission</b> a) Sent to Commission b) Date of the regulation c) OJ No.
a) Isoflurane	a) Equine	a) 13.05.96 b) 07.05.97 c) 200 days d) 158 days	a) 05.06.97 b) 23.02.98 c) OJ No. L 53 of 24.02.98
a) Teflubenzuron	a) Fish	a) 20.01.97 b) 07.05.97 c) 105 days d) 0	a) 05.06.97 b) 23.02.98 c) OJ No. L 53 of 24.02.98
a) Florfenicol (extension)	a) Fish	a) 29.01.96 b) 16.07.97 c) 129 days d) 404 days	a) 12.08.97 b) 18.03.98 c) OJ No. L 82 of 19.03.98
a) Moxidectin (extension)	a) Equidae	a) 09.04.97 b) 16.07.97 c) 96 days d) 0	a) 12.08.97 b) 18.03.98 c) OJ No. L 82 of 19.03.98
a) Praziquantel (extension)	a) Equidae	a) 15.09.97 b) 14.01.98 c) 120 days d) 0	a) 09.02.98 b) 27.05.98 c) OJ No. L 154 of 28.05.98
a) Meloxicam	a) Bovine	a) 28.03.96 b) 11.06.97 c) 212 days d) 229 days	a) 09.07.97 b) 17.07.98 c) OJ No. L 205 of 22.07.98
a) Tilmicosin (extension)	a) Chicken	a) 14.07.97 b) 12.11.97 c) 111 days d) 0	a) 12.12.97 b) 09.09.98 c) OJ No. L 250 of 10.09.98
a) Valnemulin	a) Porcine	a) 02.08.96 b) 06.05.98 c) 207 days d) 435 days	a) 05.06.98 b) 27.11.98 c) OJ No. L 320 of 28.11.98
a) Alfaprostol (extension)	a) Rabbits	a) 15.05.97 b) 06.05.98 c) 200 days d) 156 days	a) 05.06.98 b) 27.11.98 c) OJ No. L 320 of 28.11.98
a) Rifaximin	a) All mammalian food producing species	a) 09.01.97 b) 06.05.98 c) 180 days d) 303 days	a) 05.06.98 b) 27.11.98 c) OJ No. L 320 of 28.11.98
a) Bronopol	a) Salmonidae	a) 07.05.97 b) 10.06.98 c) 198 days d) 202 days	a) 10.07.98 b) 11.12.98 c) OJ No. L337 of 12.12.98
a) Flumethrin	a) Bovine, Ovine, Caprine, Honey bees	a) 11.11.96 b) 10.06.98 c) 197 days d) 380 days	a) 10.07.98 b) 11.12.98 c) OJ No. L 337 of 12.12.98
a) Enrofloxacin (modification)	a) Bovine, Porcine, Poultry	a) 03.02.97 b) 08.07.98 c) 183 days d) 336 days	a) 30.07.98 b) 17.12.98 c) OJ No. L 343 of 18.12.98
a) Enrofloxacin (extension)	a) Dairy cattle, Ovine, Rabbits	a) 03.02.97 b) 08.07.98 c) 183 days d) 336 days	a) 30.07.98 b) 17.12.98 c) OJ No. L 343 of 18.12.98

<b>Substance</b> a) INN	<b>Therapeutic area</b> a) Target species	<b>EMEA/CVMP</b> a) Validation b) Opinion c) Active time d) Clockstop	<b>Commission</b> a) Sent to Commission b) Date of the regulation c) OJ No.
a) Sodium 2-methyl-2-phenoxy-propionate	a) Bovine, Porcine, Caprine, Equidae	a) 26.11.96 b) 08.07.98 c) 201 days d) 388 days	a) 30.07.98 b) 17.12.98 c) OJ No. L 343 of 18.12.98
a) Ivermectin (extension)	a) Deer	a) 20.08.96 b) 08.07.98 c) 170 days d) 518 days	a) 30.07.98 b) 17.12.98 c) OJ No. L 343 of 18.12.98
a) Diethylene glycol monoethyl ether	a) Bovine, Porcine	a) 14.02.97 b) 08.07.98 c) 170 days d) 337 days	a) 30.07.98 b) 17.12.98 c) OJ No. L 343 of 18.12.98

**Maximum Residue Limits for Old Substances adopted by the CVMP and the Community**  
(Status: January 1999)

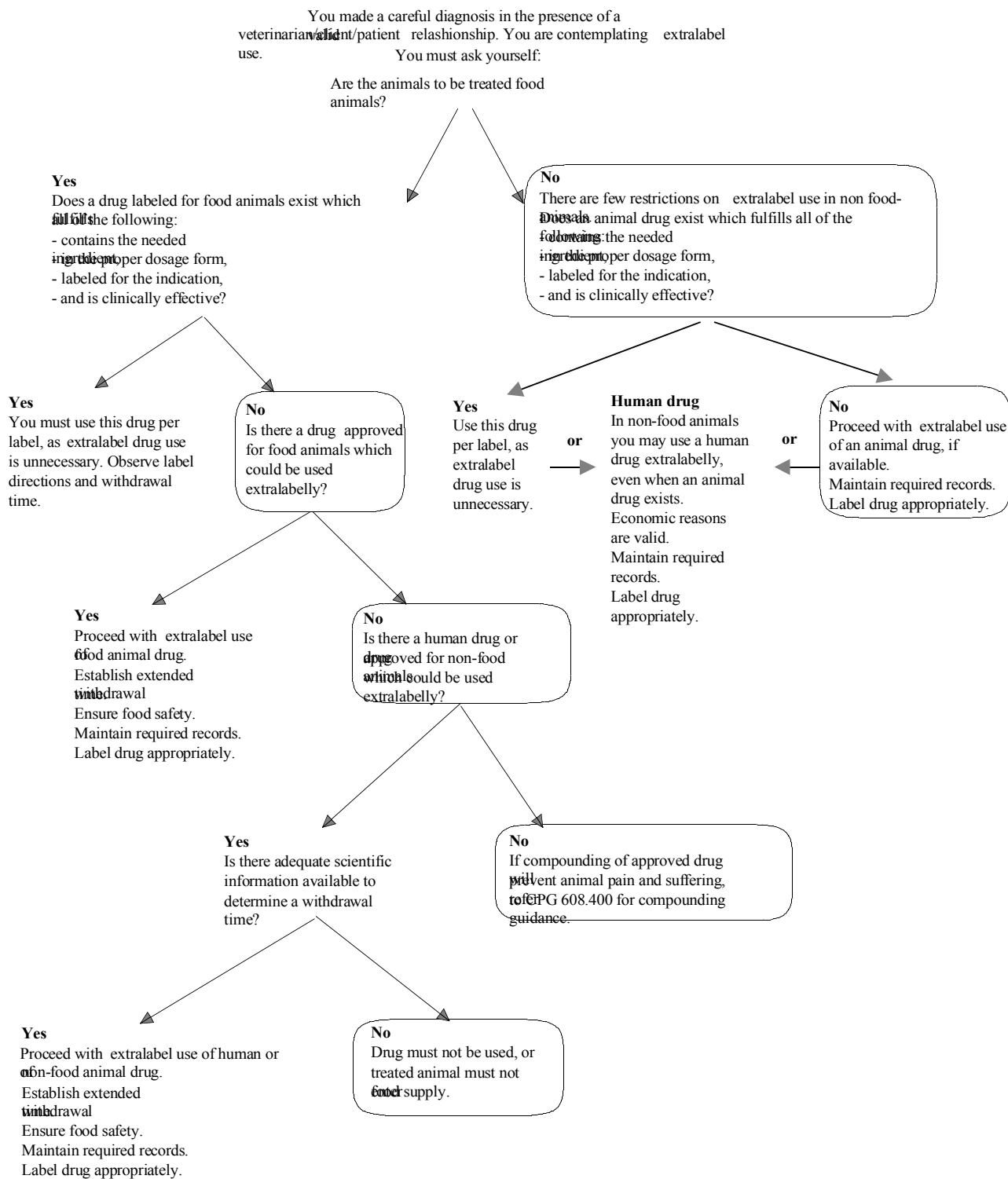
<b>TOTAL 464</b>			
<b>Annex I</b>	<b>Annex II</b>	<b>Annex III</b>	<b>Annex IV</b>
54	354	45	11
Published in the Official Journal of the European Communities: 388			

**Veterinary Medicinal Products that have been granted a Community marketing authorisation  
under the centralised procedure  
(Status: January 1999)**

<b>Product</b> a) Brandname b) INN c) Part A/B	<b>Company</b> a) Name b) Origin	<b>Therapeutic area</b> a) Target species b) Indication	<b>Presentation</b> a) Form b) Dosage c) No. Of presentations	<b>EMEA/CVMP</b> a) Validation b) Opinion c) Active time d) Clockstop	<b>Commission</b> a) Opinion received b) Decision c) Notification d) OJ No.
a) Nobivac-Porcocoli b) Inactivated vaccine c) Part A	a) Intervet International b) NL	a) Piglets b) Neonatal colibacillosis	a) Solution for injection b) Multidose c) 2	a) 01.01.95 b) 27.07.95 c) 107 days d) 94 days	a) 24.08.95 b) 29.02.96 c) 04.03.96 d) OJ No. C96 of 29.03.96
a) Pentofel b) Vaccine c) Part A	a) Fort Dodge Laboratories b) IRL	a) Cats b) Rhinotracheitis	a) Solution for injection b) Monodose c) 3	a) 16.06.95 b) 18.09.96 c) 208 days d) 235 days	a) 17.10.96 b) 05.02.97 c) 06.02.97 d) OJ No. C63 of 28.02.97
a) Quadrisol b) Vedaprofen c) Part B	a) Intervet International b) NL	a) Horses b) Control of inflammation	a) Oral gel b) 100mg/ml c) 1	a) 07.05.96 b) 16.07.97 c) 209 days d) 235 days	a) 14.08.97 b) 04.12.97 c) 05.12.97 d) OJ No. C392 of 24.12.97
a) Dicural b) Difloxacin c) Part B	a) Fort Dodge Animal Health b) NL	a) Poultry b) Antibacterial for systematic use	a) Oral solution b) 100mg/ml c) 2	a) 06.12.95 b) 11.06.97 c) 218 days d) 337 days	a) 11.07.97 b) 16.01.98 c) 20.01.98 d) OJ No. C63 of 27.02.98
a) Clomicalm b) Clomipramine c) Part B	a) Ciba-Geigy b) FR	a) Dogs b) Treatment of anxieties	a) Tablets b) 5, 20 and 80mg c) 3	a) 13.11.96 b) 12.11.97 c) 210 days d) 156 days	a) 12.12.97 b) 01.04.98 c) 02.04.98 d) OJ No. C126 of 24.04.98
a) Neocolipor b) Inactivated vaccine c) Part A	a) Rhône-Mérieux b) FR	a) Piglets b) Passive immunisation against neonatal colibacillosis	a) Suspension for injection b) 2ml c) 5	a) 02.10.96 b) 10.12.97 c) 191 days d) 245 days	a) 09.01.98 b) 14.04.98 c) 15.04.98 d) OJ No. C126 of 24.04.98
a) Nobilis IB4-91 b) Live vaccine c) Part B	a) Intervet International b) NL	a) Poultry, chicken b) Live vaccine against infectious bronchitis	a) Solution b) 30ml/1000 doses c) 5	a) 16.10.96 b) 12.11.97 c) 210 days d) 184 days	a) 12.12.97 b) 09.06.98 (corrigendum 05.08.98) c) 10.06.98 d) OJ No. C200 of 26.06.98
a) Suvaxyn Aujeszky 783+ O/W b) Live vaccine c) Part A	a) Solvay Duphar b) NL	a) Pigs b) Vaccine against Aujeszky disease	a) Solution for injection b) 2ml c) 3	a) 19.10.96 b) 08.04.98 c) 208 days d) 328 days	a) 08.05.98 b) 07.08.98 c) 10.08.98 d) OJ No. C269 of 28.08.98

# ANNEX V

## US EXTRA-LABEL USE DECISION TREE



## ANNEX VI

### MOLECULES MOST COMMONLY USED IN EQUINE MEDICINE

#### NERVOUS SYSTEM

##### ANALGESICS

**Opiates** are the only group of potent analgesics. They are essential for welfare and good standard of patient care. They are also used in combination with sedatives to produce unequalled degree of sedation for wide range of procedures. They have revolutionised safety, ease and welfare for many procedures.

Chemical Name	MRL status
Methadone	Not defended
Morphine	Not defended
Pethidine	Not defended
Butorphanol	Annex II

**Non Steroidal Anti Inflammatory Drugs (NSAIDs)** form the other major group of analgesics. They are generally less potent analgesics but cause no central depression. They are often use in sick animals and not displace the need for opiate analgesia. In severe pain opiates and NSAIDs act synergistically.

Chemical Name	MRL status
Flunixin	Defended
Carprofen	Annex III
Ketoprofen	Annex II
Phenylbutazone	Prohibited since 1.1.98
Vedaprofen	Annex I
Eltenac	Annex II
Tolfenamic acid	Defended
Mefenamic acid	Not defended

##### TRANQUILLISERS AND SEDATIVES

**Alpha-2 adrenoreceptor agonists** are mainly used for deep sedation and some of them for analgesia. They allow a wide range of procedures to be performed non-stressfully for the animals and safely for the handler.

Chemical Name	MRL status
Xylazine	Defended
Detomidine	Annex II
Romifidine	Annex II
Atipamezole*	Not defended

\*Antagonist

**Benzodiazepines** provokes mild sedation but no side effects. They are essential for sick animals and those that have aberrant reactions to alpha-2 agents and acepromazine.

Chemical Name	MRL status
Diazepam	Not defended
Climazolam	Not defended

**Phenothiazines** are very widely used, in particular acepromazine. They can be combined with antimuscarini agents when stress related functional motility disturbances or other psychogenic causes of diarrhea are suspected..

Chemical Name	MRL status
Chlorpromazine	Annex IV
Acepromazine	Defended

## GENERAL ANAESTHETICS

**Volatile agents** are essential for maintenance of anaesthesia.

Chemical Name	MRL status
Halothane	Not defended
Isoflurane	Annex II
Sevoflurane	Not defended

**Gaseous agents** are also essential for maintenance of anaesthesia.

Chemical Name	MRL status
Oxygen	Not defended
Nitrous oxide	Not defended

**Barbiturates** have been used for many years for intravenous induction of anaesthesia in all species.

Chemical Name	MRL status
Thiopentone	Not defended
Pentobarbitone	Not defended
Methohexitone	Not defended

**Cyclohexidines** are general anaesthetics with minimal depressant properties and wide safety margin. They can be given by intramuscular injection where barbiturates must be given intravenously.

Chemical Name	MRL status
Ketamine	Annex II
Tiletamine	Not defended

**Propofol** is a new intravenous anaesthetic that has near ideal properties for induction, maintenance and recovery. It is one of the most widely used anaesthetics in man and small animals. It should be retained for the sake of improving safety and welfare of anaesthesia.

Chemical Name	MRL status
Propofol	Not defended

**Chloral hydrate** is an old drug that has stood the test of time. Its effect is dose dependant: from sedation to general anaesthesia. It can provoke a profound sedation similar to alpha-2 agents that is often effective in animal resistant to the alpha-2 agents. It can be given by mouth and can therefore be used in animals that can only be sedated by an oral route and where alpha-2 agents are contraindicated.

Chemical Name	MRL status
Chloral hydrate	Not defended

## LOCAL ANAESTHETICS

Local anaesthetics are used for a wide range of surgery. There are years of experience of lignocaine and its safety and efficacy. It is also used as an anti-dysrhythmic drug. Mepivacaine is in particular used for nerve blocks in horses as there is less reactive oedema than with lignocaine in the lower limbs. Bupivacaine is also used as it is much longer acting than the others.

Chemical Name	MRL status
Lignocaine	Not defended
Bupivacaine	Not defended
Mepivacaine	Defended

## ANTICHOLINERGICS

**Anticholinergics** are used to treat and prevent side effects of general anaesthetic agents. They are essential for safe anaesthesia.

Chemical Name	MRL status
Atropine	Defended
Glycopyrrolate	Not defended

## DIGESTIVE SYSTEM

### SPASMOLYTIC AGENTS

**Antimuscarini agent** may be used as spasmolytics.

Chemical Name	MRL status
N-butyl hyoscine	Defended
Prifinium	Not defended

**Other agents** may be used as spasmolytics.

Chemical Name	MRL status
Phloroglucinol	Annex II
Metamizole	Defended

### PURGATIVE AND LAXATIVE AGENTS

**Smooth muscular stimulants** produce a fluid evacuation by increasing peristaltic activity

Chemical Name	MRL status
Neostigmine	Annex II
Oxytocine	Annex II

**Laxative agents** promote the elimination of soft formed faeces.

Chemical Name	MRL status
Mineral oil	Annex II
DSS	Annex II
Magnesium Sulfate	Annex II
Methyl Cellulose	Out of scope

### ANTIMICROBIAL AGENTS

**Anti-anaerobic drugs** are essential treatment for orthopaedic, soft tissue, abdominal or thoracic anaerobic conditions. In horses, metronidazole is the most appropriate antimicrobial for the treatment of acute toxaemic colitis.

Chemical Name	MRL status
Metronidazole	Annex IV

## CARDIOVASCULAR SYSTEM

### CARDIAC STIMULANTS

Cardiac support drugs are essential for critical care, resuscitation and maintenance of cardiac function during anaesthesia.

Chemical Name	MRL status
Dobutamine	Not defended
Dopamine	Not defended
Adrenaline	Annex II
Ephedrine	Defended
Quinidine	Not defended
Digitalis	Not defended

### PERIPHERAL VASODILATATOR

**Isosuxprine hydrochloride** is primarily needed to relief from pain and to prolong usefulness of horses which suffer from navicular disease. The use of isosuxprine for this condition is however prohibited by Council Directive 96/22/EC.

Chemical Name	MRL status
Isosuxprine	Annex II for uses authorised by Council Directive 96/22/EEC

### FLUID THERAPY

It is also essential to have use of a range of intravenous fluids for appropriate supportive therapy during anaesthesia or to treat hypovolemic shocks.

Chemical Name	MRL status
Electrolyte solutions	Annex II?
Colloid solutions	Annex II?
Hypertonic solutions	Annex II?

## MUSCULAR SYSTEM

### NEUROMUSCULAR BLOCKING AGENTS

**Peripheral acting skeletal muscle relaxants** are used as essential components of balanced anaesthesia. They are indicated to achieve muscle relaxation of the operative field.

Chemical Name	MRL status
Atracurium	Not defended
Vecuronium	Not defended
Edrophonium*	Not defended

\* Antagonist